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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/385,114	08/27/99	WHITEHOUSE M	1543.004/121

HM12/0512

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EXAMINER	
ROBINSON, H	
ART UNIT	**PAPER NUMBER**
1653	6

DATE MAILED: 05/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/385,114	Whitehouse
Examiner	**Group Art Unit**
Hope Robinson	1653

☒ Responsive to communication(s) filed on *Jan 24, 2000* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-34* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-34* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4 and 5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities:

The specification on page 21 (line 28) has the word patient spelled incorrectly as "patent". Correction is required.

Abstract

2. The abstract is objected to because it has too long. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9 appear to contain a recitation of a composition made of one active ingredient where the ingredient is referred to in the alternative but should be recited as being selected from the group consisting of (i.e., Claim 1).

Claims 10 and 17 and the dependent claims to each are indefinite as to the effect and end result of the recited treatment nor is it apparent from the claims what the step of administering consists of. What for example, are the conditions of "safe".

Claims 19-21 are indefinite for reciting "therapeutic benefit", because it is unclear what the benefit is or how much change is considered to be beneficial since it is not defined in the claim. The dependent claims are included in this rejection.

Claim 26 and the claims dependent thereto are indefinite as it is not clear how the resultant angiogenesis is limited to "heart" absent isolation of the product administered to solely heart.

Claim 30 is indefinite as to the resultant effect of the treatment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-9 are rejected under 35 U.S.C. 103(b) as being anticipated by Baird et al. (U.S. Patent No. 5,155,214, October 13, 1992).

Baird et al. disclose substantially pure mammalian basic fibroblast growth factors. Further the amino acid residue sequences of bovine and human bFGF are disclosed as well as a DNA chain encoding the polypeptide of the bovine species (see abstract). Baird et al. teach that basic FGF has a similar activity in vivo on capillary endothelial cells, therefore, basic FGF is considered

an angiogenic factor (see column 1). The reference discloses pharmaceutical compositions including bFGF, a bFGF analog, biologically active fragments of bFGF or of analog bFGF, or nontoxic salts thereof dispersed in a pharmaceutically acceptable liquid or solid carrier. In addition, the reference teaches that these pharmaceutical compositions can be used in clinical medicine, both human and veterinary, in acute or chronic administration of diagnostic or therapeutic purposes (see column 3). Baird et al. teach the sequence contained in SEQ ID No. 2 with a 100% identity to the sequence in the instant application (see alignment). Therefore, the limitations of the claims are met by this reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-34 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Baird et al. (U.S. Patent No. 5,155,214, October 13, 1992) in view of Sellke et al. (The Society of Thoracic Surgeons, vol. 65, pages 1540-1544, 1998) and Uchida et al. (American Heart Journal, vol. 130, no. 6, pages 1182-1188, December 1995).

The teachings of Baird et al. as applied to Claims 1-9 are above. Baird et al. do not expressly teach a method of for treating coronary heart disease or myocardial infarction. Sellke et al. disclose results and technical considerations of the administration of basic fibroblast growth factor for the induction of collateral growth using heparin-alginate slow-release devices in patients undergoing coronary artery by pass grafting. The reference teaches that patients with severe symptomatic coronary artery disease or coronary artery by pass grafting present a difficult clinical problem. In addition, Sellke et al. assert that therapeutic angiogenesis using naked DNA plasmids encoding angiogenic growth factors, DNA delivered by an adenoviral or liposomal vector, or the administration of authentic growth factor proteins has been advocated to improve perfusion in ischemic regions of myocardium and in patients with peripheral vascular disease. Although both gene transfection and growth factor protein delivery have relative advantages and disadvantages, the delivery of the protein as opposed to the DNA encoding the protein has a potential advantage of simplicity, consistent delivery and safety. Basic fibroblast growth factor (bFGF), a 16-kD single chain peptide has both angiogenic and mitogenic potential. Sellke et al. disclose that it has been demonstrated that the angiogenic effect of bFGF is dose dependent (see page 1540). Additionally, Sellke et al. demonstrated the safety and technical feasibility of therapeutic angiogenesis with basic fibroblast growth factor delivered by heparin-alginate slow release devices (see pages 1540-1541).

Uchida et al. teach that angiogenesis and myocardial salvage occur illustrated by, injection through the right atrium into the pericardial cavity of 30mg basic fibroblast growth factor and

3mg heparin sulfate. Uchida et al. assert that FGFs act as regulatory proteins that induce the proliferation of a variety of cells and function as an angiogenic factor in vitro and in vivo. Uchida et al. disclose that a significant increase in the number of collateral vessels and subsequent salvage of the infarcted myocardium induced by intracoronary injection of bFGF. Uchida et al. assert that the ability to administer bFGF selectively and safely into the infarcted area, irrespective of the coronary anatomy and contraindications for coronary interventions, this method can be widely applied as a therapeutic regimen for myocardinal salvage to the patients with acute myocardinal infarction or as a preventive regimen for myocardial infarction.

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole by combining the teachings of the above references because Baird et al. teach the sequence contained in SEQ ID NO. 2 for FGF-2 with a 100% identity and an angiogenically active fragment, Sellke et al. teach a method using bFGF for treating coronary artery disease and disclose the benefits of using bFGF and Uchida et al. teach an angiogenic therapy for acute myocardial infarction using bFGF. Uchida et al. also disclose that in patients bFGF injected into the coronary artery may not reach the infarcted area, because it may be conjugated with the extracelluar matrix at the site of coronary lesion or may enhance stenosis. Therefore, by administration of bFGF selectively and safely into the infarcted area, irrespective of the coronary anatomy and contraindications for coronary interventions, this method can be widely applied as a therapeutic regimen (see page 1182). One of ordinary skill in the art would be motivated to produce a unit dose composition to be delivered in these areas for treatment of

coronary artery disease and myocardial infarction based on the benefits described by Sellke et al. and Uchida et al. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Art of *Record*

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Arakawa et al. (WO 89/04832, June 1, 1989). Arakawa et al. disclose a recombinant fibroblast growth factor analogs possessing part or all of the primary structural conformation and one or more of the biological properties of a mammalian (i.e. human) basic fibroblast growth factor. The reference also teach a process for producing such analogs wherein a host cell is transformed or transfected with an exogenous DNA sequence encoding for the basic fibroblast growth factor analogs. Purification methods for the analogs are also disclosed (see abstract). Arakawa et al. teach that the heparin binding property of the factors has facilitated their purification.

Kato et al. (U.S. Patent No. 5,314,872, May 24, 1994). Kato et al. teach fibroblast growth factor or a mutein of FGF. The composition comprising FGF or a mutein of FGF and a glucan sulfate is stabilized so that it can be advantageously administered to warm blooded animals.

7. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday-Friday from 9:00 am to 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MS

Patent Examiner

Christopher S.F. Low

CHRISTOPHER S.F. LOW
SUPERVISORY PATENT EXAMINER
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